Title: **Mapping the brain correlates of borderline personality disorder: a functional neuroimaging meta-analysis of resting state studies**

Running head: **Resting state meta-analysis in borderline personality disorder**

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Abstract

Altered intrinsic function of the brain has been implicated in Borderline Personality Disorder (BPD). Nonetheless, imaging studies have yielded inconsistent alterations of brain function. To investigate the neural activity at rest in BPD, we conducted a set of meta-analyses of brain imaging studies performed at rest. A total of seven functional imaging studies (152 patients with BPD and 147 control subjects) were combined using whole-brain Signed Differential Mapping meta-analyses. Furthermore, two conjunction meta-analyses of neural activity at rest were also performed: with neural activity changes during emotional processing and with structural differences, respectively. We found altered neural activity in the regions of the default mode network (DMN) in BPD. Within the regions of the core DMN, patients with BPD showed greater activity in the anterior as well as in the posterior midline hubs relative to controls. Conversely, in the regions of the dorsal DMN they showed reduced activity compared to controls in the right lateral temporal complex and in bilateral orbitofrontal cortex. Increased activity in the precuneus was observed both at rest and during emotional processing. Reduced neural activity at rest in lateral temporal complex was associated with smaller volume of this area.

Altered activity in the regions of the midline core as well as of the dorsal subsystem of the DMN may reflect difficulties with interpersonal and affective regulation in BPD. These findings suggest that changes in spontaneous neural activity could underlie core symptoms in BPD.

Keywords: borderline personality disorder; magnetic resonance imaging; resting state; positron emission tomography; meta-analysis

Introduction

Borderline Personality Disorder (BPD) is a severe mental disorder characterized by a heterogeneous constellation of psychiatric symptoms which can be mainly grouped in the following dimensions: “Disturbed relatedness”, referring to a pattern of unstable relationships, identity disturbance, chronic sense of emptiness and stress-related paranoid thoughts; “Behavioral dysregulation”, including impulsive and self-injurious behaviors; and “Affective dysregulation”, entailing affective instability, inappropriate anger and strenuous efforts to avoid abandonment (Sanislow et al., 2002).

Functional neuroimaging research has provided increasing insight into the neural correlates of BPD (Leichsenring et al., 2011). Recent meta-analyses on disturbed emotion processing in BPD reported a consistent pattern of altered function and structure in cortical regions, including prefrontal cortex (PFC), and temporal cortex, along with limbic regions, i.e., amygdala and insula (Ruocco et al., 2013; Schulze et al., 2016). These findings suggest that fronto-limbic dysfunction (i.e., reduced fronto-cingulate activity leading to limbic hyperactivity) could underlie affective dysregulation in BPD (Ruocco et al., 2013). Although convergent to a certain extent, the results of the functional imaging studies carried out for this disorder are heterogeneous. Several factors in the study samples could contribute to such heterogeneity including age, gender distribution, clinical severity, comorbidities, history of trauma, and medication status (Schulze et al., 2016). Most importantly, the measurement of brain activity during the performance of a task is inherently biased by the experimental condition that is being tested. Indeed, most studies on BPD focused on identifying altered brain activity associated with affective dysregulation (Kernberg, 1984; Linehan, 1993), thus constraining the spatial distribution of the altered neural activity to fronto-limbic regions involved in emotional processing and regulation. Furthermore, issues related to different behavioral performance at the task at hand (Ruocco, 2005), strategies (Gvirts et al., 2015), motivation (Saunders et al., 2015), focus and sustained attention (Posner et al., 2002) could

contribute to intra-individual variability and reflected in changes of neural activity (Kaiser et al., 2008).

Resting state functional imaging can allow the study of spontaneous ("intrinsic") neural activity. Compared to its reflexive function that bears a very small energetic cost (<5%), intrinsic activity accounts for most of the total energy consumption of the brain (Raichle and Mintun, 2006). Different imaging techniques could be used to assess intrinsic neural activity at rest, including fluoro-deoxy-glucose (FDG)- Positron Emission Tomography (PET) or single-photon emission computed tomography (SPECT), which allow a direct estimation of cerebral metabolism, and blood oxygenation level-dependent (BOLD) functional Magnetic Resonance Imaging (fMRI) which can indirectly measure neural activity via hemodynamic changes. During resting state not only local differences of neural activity, but also changes of functional coupling between brain regions could be estimated This latter measure, which is known as functional connectivity, is most frequently calculated using seed-based connectivity that is susceptible to observational biases depending on the location and the definition of the seed, thus making these studies less amenable to undergo a meta-analysis. For this reason we did not include these studies in the present paper. Notably, recent literature has shown similar spatial extent between patterns of brain intrinsic activity measured with these techniques (Riedl et al., 2014). Intrinsic networks estimated at rest have also been associated with behavioral indexes (Smith et al., 2009; Visintin et al., 2015). Thus, the study of resting state activity can be useful to investigate brain function relevant to behavior but without the confounding effects of task performance itself.

Among several brain networks, the default mode network (DMN) is particularly modulated by rest/task conditions. Indeed, the DMN spans across a set of brain areas that are more active at rest than during a goal-directed task (Raichle et al., 2001). The DMN can play a role in emotional, self-referential processing, memory and attentional processing (Andrews-Hanna et al., 2014), which are all functions known to be altered in BPD. This network is composed

by a number of subcomponents with specific functions, including a midline core, a dorsal, and a ventral subsystem (Andrews-Hanna et al., 2014; Sambataro et al., 2014). In particular, the midline core of the DMN, spanning across the medial prefrontal cortex and the precuneus/posterior cingulate is associated with self-related (self-referential, autobiographical) and emotional processing, which are dysfunctional in the “affective dysregulation” as well as in the “disturbed relatedness” factors of BPD. The dorsal DMN subsystem, which also comprises several regions of the temporal cortex (i.e., temporo-parietal junction, lateral temporal cortex and temporal poles), has been associated with social communication and cognition, as well as language processing which are functions altered in the “disturbed relatedness” (Andrews-Hanna et al., 2014). The ventral subsystem entails the hippocampal formation, retrosplenial cingulate cortex, the ventral portion of the medial prefrontal cortex. These regions are recruited during autobiographical memory, associative memory, semantic and conceptual knowledge, and spatial information that may be associated with altered “disturbed relatedness” factor as well as with the cognitive alterations of BPD (Ruocco, 2005). Altered engagement of the DMN has been reported not only in BPD (Wolf et al., 2011), but also in depression (Sambataro et al., 2014), bipolar disorders (Martino et al., 2016), and schizophrenia (Sambataro et al., 2010) that are disorders with clinical similarities with BPD.

In addition, structural changes could affect functional results in BPD. A recent meta-analysis on 10 whole brain volume-based morphometric studies identified substantial volumetric gray matter differences in a widespread pattern of brain regions including-frontolimbic regions in 263 patients with BPD relative to 278 healthy controls (HC) (Schulze et al., 2016). In particular, patients had greater PFC and cerebellar volume along with reduced hippocampal, temporal, occipital and lateral prefrontal volumes, and some of these changes overlapped with functional imaging changes during emotional processing. Underlying structural regional changes may result in functional differences measured using functional imaging in the same

brain areas (Dukart and Bertolino, 2014). The identification of the spatial overlap of these changes could be useful to isolate the regions that are primarily affected in BPD.

The aim of this meta-analytic study was to identify quantitatively the intrinsic neural functional changes associated with BPD diagnosis. To do so, we first performed a meta-analysis to identify the effect of BPD diagnosis on functional neuroimaging responses by integrating existing results across multiple resting state modalities. Second, given the role altered affective regulation in BPD symptoms we wanted to identify the overlap between functional activity changes at rest and during emotional processing in BPD. For this aim we performed a conjunction meta-analysis with the results reported in the largest whole brain meta-analysis of the functional changes associated with negative emotional processing (Schulze et al., 2016). The meta-analysis by Schulze and coworkers included 19 whole brain functional imaging studies investigating the brain activity during tasks probing negative emotional processing. In particular, the contrasts of the negative versus neutral emotion condition were compared between 281 patients with BPD and 293 HC. Third, to identify the overlap between functional activity changes at rest and altered morphometry in this disorder, we used a conjunction multimodal meta-analysis with the result of a recent volumetric gray matter changes meta-analysis in BPD (Schulze et al., 2016, see above). Furthermore, we assessed the contribution of resting state neuroimaging modality (PET vs fMRI) on intrinsic neural activity differences measured at rest.

Materials and methods

Article selection and classification. We performed a literature search using PubMed to identify functional neuroimaging studies of resting state in BPD in English language published between January 2000 and January 2016 (Figure 1). The following search terms were used: “borderline AND resting state” and retrieved 57 articles.

We also explored results from broader search entries such as: “MRI AND borderline personality disorder”, “PET AND borderline personality disorder”, “SPECT AND borderline personality disorder” to detect additional resting state studies.

After a review of the abstracts of these articles, 13 studies were selected for full-text reading. References cited in the selected articles were also reviewed. We included only papers that reported stereotaxic coordinates of contrasts comparing patients with BPD and HC resulting from whole-brain analyses. Independent Component Analysis (ICA) studies were included when analyzing multiple large-scale brain networks. Seed-based connectivity and low frequency oscillation studies, and articles that were not resting state studies were excluded. When multiple studies or experiments investigated overlapping group of patients (Wolf et al., 2011; Wolf et al., 2012), we included only the study (Wolf et al., 2011) with the largest sample (34 vs. 32 participants). For each of the 7 papers finally selected, we extracted demographic and clinical information (Table S.1) along with the coordinates of significant foci for the BPD vs. HC comparisons. The total number of participants included was 152 BPD and 147 HC. The final set of coordinates resulted in 39 foci: 23 for BPD>HC and 16 for HC>BPD contrast, respectively (Table S.1). The instructions for resting state scan were different across studies: two studies requested eyes open condition, three eyes closed, and two studies did not specify instructions (see table S.2, for more details).

Meta-analyses. First, we conducted a meta-analysis to identify the main effect of BPD diagnosis on task-independent neural function. Second, we carried out two further meta-analyses based on the imaging modality: fMRI studies (Das et al., 2014; Doll et al., 2013; Salvador et al., 2016; Wolf et al., 2011) and PET studies (Lange et al., 2005; Salavert et al., 2011; Soloff et al., 2005) (Table S.1). Meta-analyses were performed separately for the BPD>HC and the HC>BPD contrasts using SDM software (Signed Differential Mapping, www.sdmproject.com). Coordinates in MNI or Talairach and Tournoux systems were

extracted, along with t-values. Where only p or z-values were available, we used the online "Two-sample z/p to t converter" available on the SDM website. All the meta-analyses were performed using the anisotropic effect-size-based algorithms (AES-SDM) (Radua et al., 2012; Radua et al., 2014). The new version of SDM software allows the use of both the positive features of existing peak-probability methods (such as activation likelihood estimation) and of image-based meta-analyses, using standard effect size and variance-based meta-analytic calculations. SDM uses peak coordinates to reconstruct (to a limited extend) the original maps, thus taking into account both positive and negative differences (e.g. increased and reduced neural activity).

When peak coordinates are used to recreate the effect-size brain maps of the original studies, voxels from these brain maps are randomly permuted to create Monte Carlo brain maps, useful for estimating the null distributions of the subsequent analyses. We chose to perform 500 permutations. The results from the global and the imaging technique-specific meta-analyses were thresholded with a $p<0.005$, $|SDM\text{-}Z|>1$ and a spatial extent of 20 voxels as detailed elsewhere (Schulze et al., 2016). Images were displayed on a standardized anatomical template in MNI space (ch2.nii) using MRIcron (www.mccauslandcenter.sc.edu/mricro/mricron/). Between-study heterogeneity estimates were calculated to examine which brain regions yielded heterogeneous measurement of activity across studies. The robustness of the results was assessed using Jackknife sensitivity analysis, which consists of repeating the main statistical analysis N times (where N is the number of studies) discarding one different study each time. If a brain region remains significant in all or most of the combinations it can be concluded that its finding is highly robust. Finally, we extracted values from relevant peaks and their funnel plots were built using R (www.r-project.org; see supplementary materials).

To ascertain the relationship between altered brain activity at rest and emotional processing in BPD, we performed a conjunction analysis between the global resting state meta-analysis

and the probability map of the whole-brain meta-analysis of functional changes during negative emotional processing in BPD (Schulze et al., 2016). Furthermore, to identify whether our findings could be associated with underlying structural changes we performed a conjunction analyis between the global resting state meta-analysis and the probability map of the whole brain meta-analysis on gray matter changes in BPD (Schulze et al., 2016). The meta-analysis maps from Schulze's study were thresholded as in the current paper (see above). These maps were retrieved on March 25, 2016 (after a publication erratum was issued) from the following repository: http://neurovault.org/collections/TDPEZUJL/. Each conjunction analysis resulted in a single analytical map estimated using SDM software. For this analysis, a statistical threshold corrected for the number of comparisons of p=.0025 (=.005/4 = two contrasts and two imaging modalities) was used.

Results

Global meta-analysis

Hyperactivity was identified in patients with BPD relative to HC in the medial prefrontal cortex (mPFC)/anterior cingulate (aCC) and precuneus/posterior cingulate (PreC/PCC) (Table 1 and Figure 2). Some voxels within these clusters showed heterogeneity (mPFC= .02%, PreC/PCC=.1%, p<.001). Furthermore, results in PreC/PCC had medium robustness. Clusters of decreased activity in BPD emerged in the right lateral temporal cortex spanning across middle and inferior temporal gyrus, and in the orbitofrontal cortex. Reduced activity was present in the dorsolateral prefrontal cortex, although with medium robustness.

fMRI studies

Among studies where multivariate methods (global brain connectivity, and independent component analysis) in resting state BOLD fMRI were applied to estimate intrinsic brain activity in BPD, we found a cluster of increased activity in the mPFC/aCC, and a cluster of

decreased activity in the right middle/inferior temporal gyrus in BPD compared to HC (Table 1 and Figure S.1). The right parahippocampus and the dorsolateral prefrontal cortex had also decreased activity in BPD, but this result had low robustness.

PET studies

Foci collected from studies that measured local activity using PET contributed significantly to a cluster of hyperactivity in the mPFC/aCC as well as in the right PreC/PCC in BPD compared to HC. The results in this latter region showed significant heterogeneity. Decreased connectivity was present in the right lateral temporal complex (Table 1 and Figure S.2).

Multimodal analyses

A cluster of reduced brain activity in BPD relative to HC, located in right middle temporal gyrus (xyz= 56, -58, 2, k=77, Fig.3.A) overlapped with reduced regional gray matter volume in BPD relative to HC. We found also a significant overlap of increased brain activity at resting state as well as during emotional processing in BPD relative to HC in the Prec/PCC (xyz= 6, -62, 22, k=50, Fig.3.A).

Discussion

Our meta-analysis revealed that in BPD, relative to controls, neural activity at rest was greater in midline regions including the medial prefrontal cortex/anterior cingulate and the precuneus/posterior cingulate, and decreased in middle/inferior temporal cortex and in orbitofrontal cortex. The results of fMRI and PET activity meta-analyses mostly overlapped with the results of the global meta-analysis and showed increased activity in medial prefrontal cortex/anterior cingulate as well as reduced activity in right middle/inferior

temporal cortex. Furthermore, in BPD precuneus/posterior cingulate activity was increased both at resting state and during emotional processing. Finally, decreased neural activity in right temporal cortex overlapped with volumetric reductions in patients with BPD compared to controls.

Overall, our findings support the idea of an altered activity of the regions spanning across the default mode network (DMN) in BPD, and in particular in the midline core as well as in dorsal subsystems.

Within the midline core, we found evidence of increased activity in the regions spanning across the anterior and the posterior hubs, medial prefrontal cortex/anterior cingulate and precuneus/posterior cingulate, respectively. Notably, medial prefrontal cortex/anterior cingulate activity is crucial for self-referential processing, for successful social cognition and interpersonal transactions (Saxe, 2006; Van Overwalle, 2009), as well as for emotional regulation (Etkin et al., 2011). Patients with BPD display various difficulties in self-related information processing. For instance, they show a negative evaluation bias for positive, self-referential information (Winter et al., 2015) and a decreased positive evaluation of self-referential social feedback (Korn et al., 2016), while at the same time they overestimate their capacity for cooperative relationships (Morey, 2014). Thus, increased medial prefrontal cortex/anterior cingulate activity at rest may contribute to this marked distortion of self-other representations and the subsequent interpersonal dysfunction exhibited by BPD patients. Consistently, individuals with BPD show increased medial prefrontal cortex/anterior cingulate activity during social interaction tasks relative to controls (Ruocco et al., 2010). Notably, our conjunction analysis failed to identify a significant overlap of increased medial prefrontal cortex/anterior cingulate activity at resting state and functional changes during negative emotional processing. Conversely, previous imaging studies on affective processing generally reported reduced/blunted medial prefrontal cortex/anterior cingulate activation (e.g., Ruocco et al., 2010). Together these findings suggest that medial prefrontal

cortex/anterior cingulate hyperactivity at rest in BPD may reflect a dysfunction of fronto-limbic circuitry, which then translates into a reduced ability to further activate these prefrontal regions during the performance of emotion processing tasks, and into the subsequent failure to effectively modulate the associated limbic hyperactivity (Ruocco et al., 2013; Schulze et al., 2016).

The posterior cingulate/precuneus is also associated with self-awareness and autobiographical memory (Andrews-Hanna et al., 2014). In patients with BPD, increased activity in the precuneus and posterior cingulate has been associated with processing affectively charged scenes (Koenigsberg et al., 2009) as well as social exclusion clues (Domsalla et al., 2014) and altered functional connectivity in these areas has been linked with disturbances in self-referential and emotional processing of pain (Kluetsch et al., 2012; Niedtfeld et al., 2012). A relative functional hyperactivity in posterior cingulate during emotion processing has been reported in BPD, possibly suggesting an increased self-relevance of negative stimuli (Schulze et al., 2016). Importantly, our conjunction analysis demonstrated a significant overlap of increased precuneus/posterior cingulate activity at rest and during affective processing. This finding can suggest an intrinsic rather than a process-dependent alteration of the neural activity in these regions. Specifically, a persistent activity of precuneus/posterior cingulate may reflect an altered ability to allocating attention; BPD patients may focus too much on autobiographical/self-referential cues (Scherpiet et al., 2014) and may have problems with switching attention from this “baseline” state to external, task-related demands (Kluetsch et al., 2012; Schulze et al., 2016). For instance, BPD patients show altered self-referential processing of social events (“hypermentalization”, (Sharp et al., 2013), which can affect both the evaluation and memory of social events and contribute to their interpersonal dysfunction; thus, they may benefit from interventions aimed toward redirecting attention from the self to others (Winter et al., 2015). Our findings further suggest that BPD patients may display a prominent self-related processing even at rest, and

suggest a potential neural correlate of this specific facet of the “disturbed relatedness” BPD factor.

Within the dorsal DMN, we found that individuals with BPD showed reduced activity in the right lateral temporal complex, including inferior temporal and middle temporal gyri, compared to controls. Specifically, the lateral temporal complex has been involved in semantic memory, language, visual perception (the “what” pathway), as well as in the integration of information from different senses (e.g., visual, haptic, and tactile; (Tompa and Sary, 2010). We found reduced activity in this complex in BPD relative to controls irrespective of the methodology of resting state studies. Alterations in this region could lead to dissociation, a prevalent and debilitating symptom in BPD that greatly contribute to the identity disturbance and dysfunctional relationships typical of BPD patients’ “disturbed relatedness”. Penfield and Rasmussen (1950) already showed dissociative experiences following the stimulation of these regions during neurosurgery. Previous studies in patients with temporal lobe epilepsy (Schenk and Bear, 1981), post-traumatic stress disorder (Mueller-Pfeiffer et al., 2013) and dissociative disorders (Saxe et al., 1992) have linked altered activity in temporal lobe including lateral regions with dissociative phenomena. Lange and colleagues have shown that patients with BPD with severe dissociative symptoms had reduced activity at rest in the lateral temporal complex and activity in this region predicted impaired memory performance (Lange et al., 2005). Consistently, structural studies in BPD have shown altered gray matter volume in middle temporal gyrus and the extent of this change predicted BPD severity (Niedtfeld et al., 2013). Lateral temporal complex is also involved in emotional processing of faces and scenes (Sabatinelli et al., 2011). A previous meta-analysis of structural changes in BPD identified a volumetric reduction in the inferior temporal gyrus (Schulze et al., 2016). Notably, our conjunction meta-analysis showed an overlap of structural and functional changes in this region, with both reduced activity at rest and gray matter volume in patients relative to controls. The mutual relationship between

these changes is not clear as structural changes can result in functional changes and viceversa. Some evidence suggests that structural changes are already present in patients with BPD in limbic but not in cortical regions during adolescence (Richter et al., 2014). The paucity of studies, small sample sizes, and gender imbalance limit the extent of these results. Multimodal approaches are warranted in the study of this disorder and longitudinal studies should investigate the timing and the dynamics of these events.

Finally, the orbitofrontal cortex is part of the affective network and is involved in emotional regulation via its reciprocal connections with the limbic system as well as in impulse control. Affective dysregulation represents the most prominent and extensively studied symptom domain of BPD. Reduced activity in the orbitofrontal cortex as identified in this meta-analysis was found not only in imaging studies (New et al., 2007; Silbersweig et al., 2007) but also with magnetoelectroencephalography (Diaz-Marsa et al., 2011). In this latter study, decreased activity in this region was associated with affective dysregulation, and particularly predicted more severe depressive symptoms and lower global functioning in BPD. Furthermore, altered activity of the orbitofrontal cortex can contribute to behavioral dysregulation dimension. Indeed, human lesion studies have implicated the orbitofrontal cortex also in impulse control via its role on time perception (Berlin et al., 2004). Patients with BPD exhibit increased impulsiveness as well as faster subjective sense of time both in terms of an overestimation and an underproduction of time intervals (Berlin et al., 2005; Berlin et al., 2004). Indeed, the overestimation of waiting time could cause higher levels of frustration which then results in increased impulsivity (Barratt, 1983). Our findings further suggest that decreased activity of orbitofrontal cortex can be detected even at rest in patients with BPD, confirming the central role of this area in the psychopathology of this disorder.

Overall, our results support a role of the brain regions within the subsystems of the default mode network in the pathophysiology of BPD. Altered spatiotemporal patterns of neural

activity present at rest in those brain regions devoted to self-related, social, emotional and memory processing can create *a priori* biases, e.g. personality traits and cognitive abilities, which then translate in altered function during a task according to the so-called spontaneous trait reactivation (STR) hypothesis (Harmelech and Malach, 2013). According to this hypothesis, correlation structure of functional activity of the brain that translates in spontaneous fluctuations of neural activity could reflect both the statistical structure of the environment filtered through memory systems (Sadaghiani and Kleinschmidt, 2013) and the individual's inner world and cognitive biases that constitute a sort of Bayesian brain priors (Friston, 2010). Following this biased probability patients are prone to show specific brain alteration also during task processing and this translates into altered behavior. More specifically, our findings point to alterations of the DMN regions that are implicated in the perception of self and others as well as in memory and affective processing in patients with BPD compared to healthy controls. The altered resting state activity within these networks could therefore underlie core symptoms of BPD that are typically observed in real life situations, such as disturbed relatedness, affective dysregulation and behavioral dysregulation.

A limitation intrinsic to meta-analytic approaches must be acknowledged. To investigate neural changes during resting state we pooled data across two imaging modalities. To assure robustness and reduce heterogeneity, we used novel and conservative statistical correction methods that allowed controlling for these problems

Psychiatric comorbidity is very common in patients with BPD and was present in the studies included in the meta-analyses. Future studies in individuals free from other psychiatric disorders are warranted to confirm the validity of these alterations as neural phenotypes for this disorder. Alternatively, studies in non-clinical samples with varying (i.e., low, mid and high) degrees of BPD traits that have no mental disorders and no psychotropic medication treatment, would help to clarify whether the brain alterations are specifically associated with

the clinical status, ultimately promoting a better understanding of the neurocognitive dimensions underlying BPD.

In conclusion, this study identified a pattern of altered activity in the regions of the core and dorsal subsystems of the DMN in BPD at rest. These intrinsic neural alterations could be core to the neurobiology and the symptoms of BPD and candidate biomarkers for this disorder. Furthermore, the pattern of neural dysfunction partially overlapped with spatial alterations in BPD. Hence, future studies should use multimodal approaches to study this disorder.

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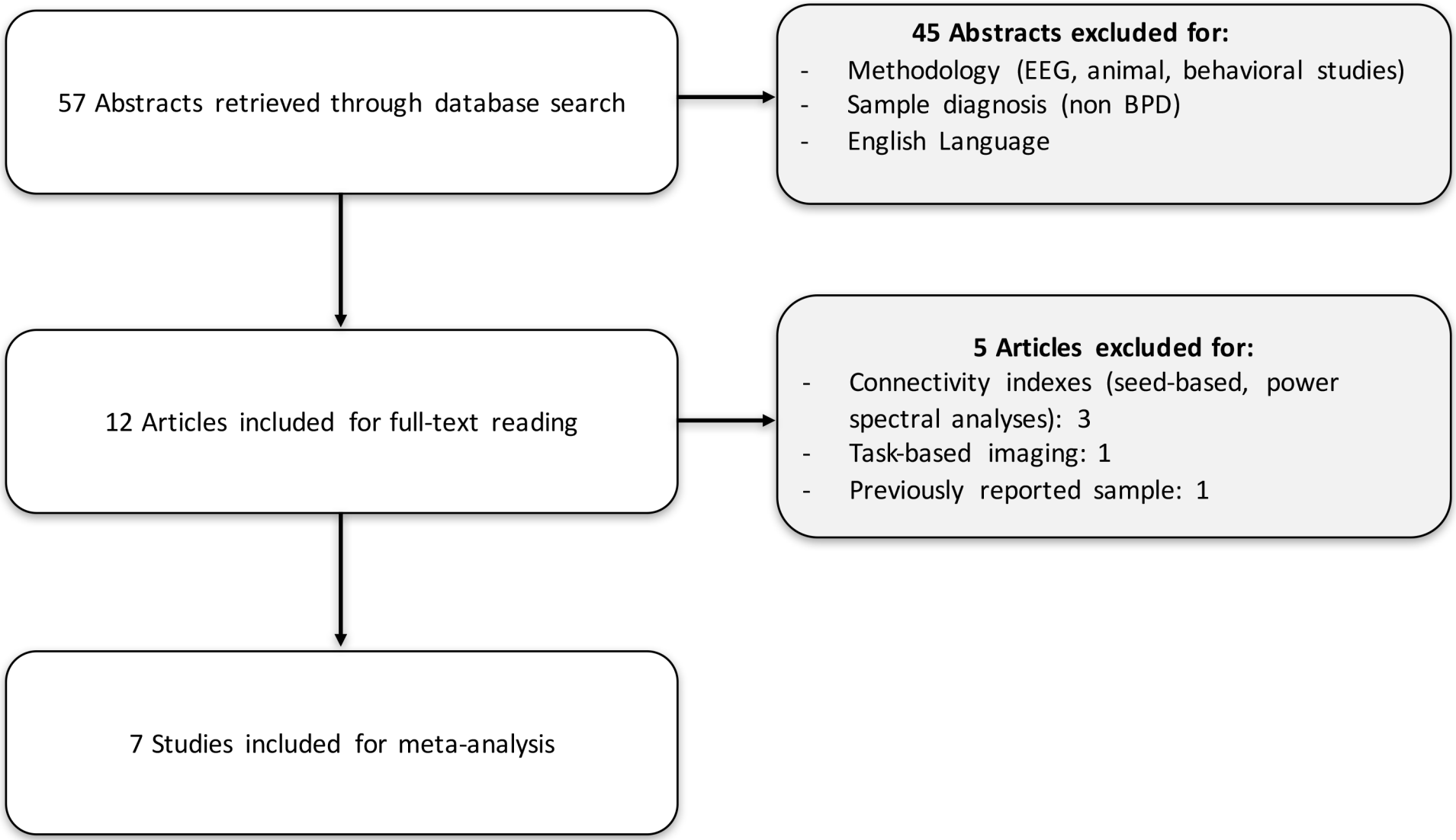
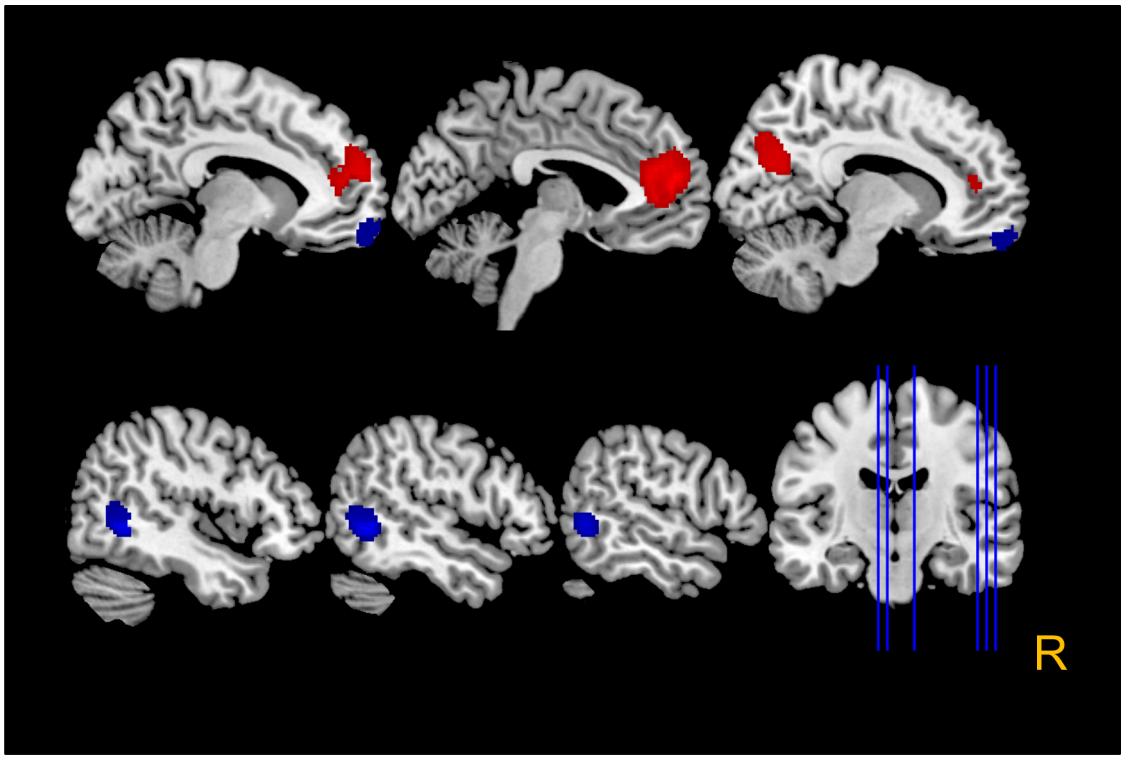
Figures

Figure 1. Article selection flow.

Figure 2. Global meta-analysis of neural activity alterations in patients with Borderline Personality Disorder (BPD) at rest. Increased (red) and decreased (blue) likelihood of functional activity differences in BPD relative to healthy controls overlaid on a sagittal view of the MNI template. Statistical images are thresholded at $p<0.005$ and $k>20$ voxels. R, right.

Figure 3. Functional and structural meta-analyses in patients with Borderline Personality Disorder (BPD). Conjunction of decreased volume and reduced functional activity at rest in BPD relative to healthy controls was significant in right middle temporal gyrus (A). Increased functional activity at rest overlapped with increased activations during emotional task in patients with BPD in precuneus (B). Statistical images are thresholded at $p<0.0025$ and $k>20$ voxels. R, right.


57 Abstracts retrieved through database search
45 Abstracts excluded for:
- Methodology (EEG, animal, behavioral studies)
- Sample diagnosis (non BPD)
- English Language
12 Articles included for full-text reading
5 Articles excluded for:
- Connectivity indexes (seed-based, power spectral analyses): 3
- Task-based imaging: 1
- Previously reported sample: 1
7 Studies included for meta-analysis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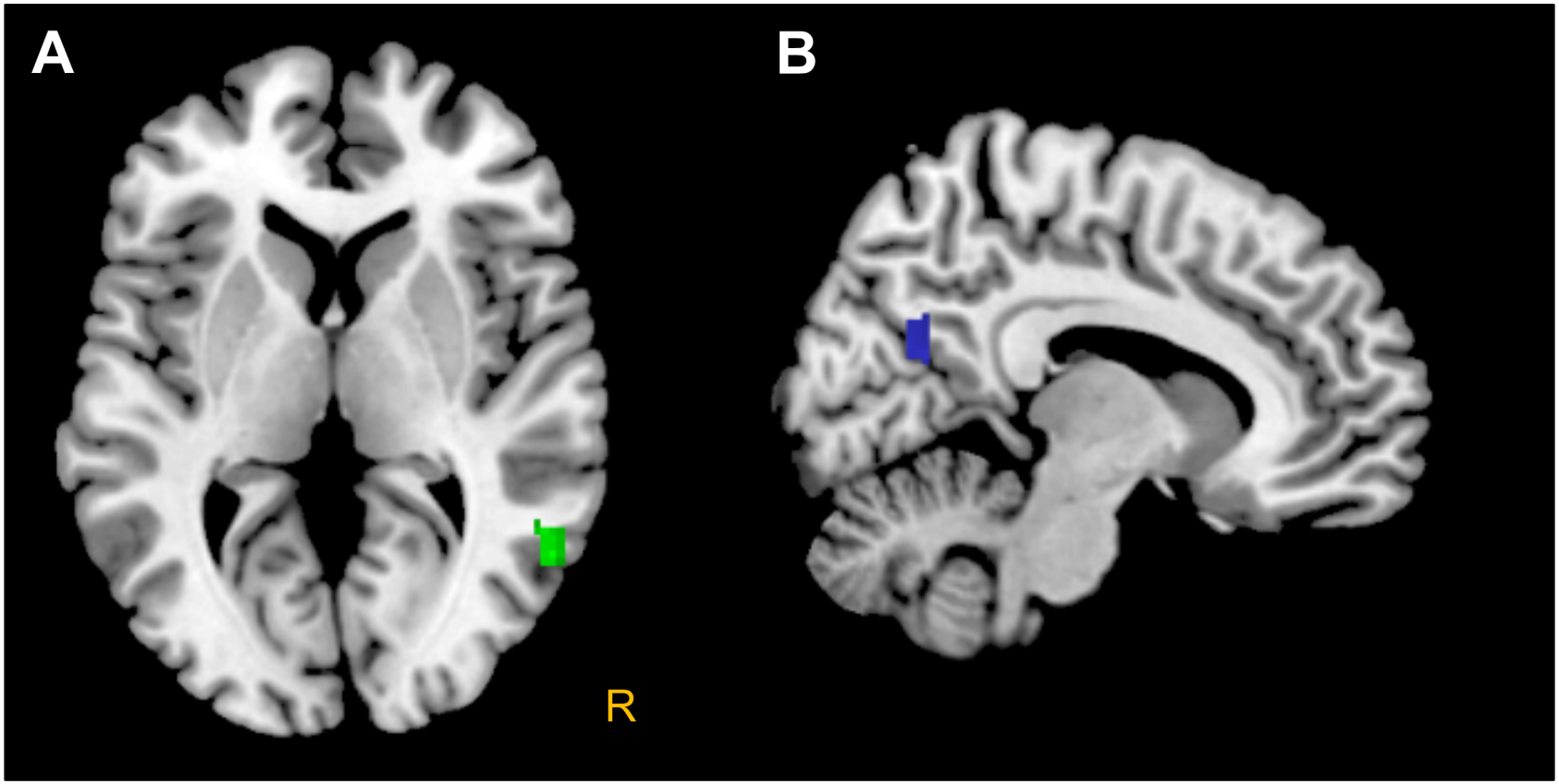
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